24 and 72h after the switch, and verified through standard Light Transmission Aggregometry (LTA).
Results: No relevant difference in platelet aggregation between the two study arms was observed at baseline (p=0.256). Residual platelet aggregation measured using MEA was significantly reduced in both arms 2h after the first administration of TICA (both p<0.001). Most interestingly, no difference in aggregation was found 2 hours after the switch to TICA (176±72 vs 181±60 AUmin, p=0.281). Similar findings were confirmed with LTA.
Conclusions: Switching from ongoing CLO therapy to TICA without a loading dose is safe and is not associated to a lower degree of PLT inhibition in patients with ACS. Larger trials are needed to confirm the present results on a clinical endpoint, as incidence of bleedings.

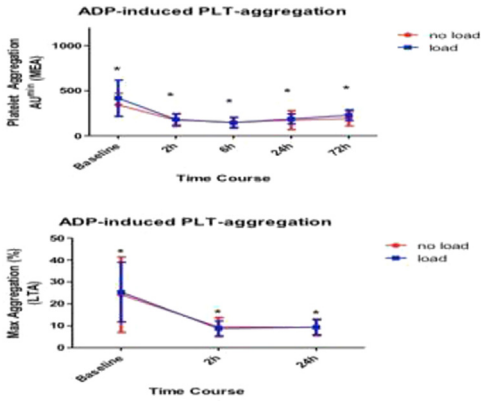

Table. Base-Case Estimates of 5-Year Treatment Costs and Quality-Adjusted Life-Years

Treatment Strategy	Germany	Italy	France	Spain	The Netherlands
Universal Ticagrelor					
Costs (€)	19,611	19,806	19,287	19,355	19,058
QALYs	3.919	3.858	3.764	3.822	3.910
PRA-Driven Ticagrelor					
Costs (€)	19,195	19,168	18,965	18,851	18,633
QALYs	3.910	3.849	3.756	3.814	3.902
ICER vs. PRA-Driven Ticagrelor	46,222	70,889	40,250	63,000	53,125
Universal Prasugrel					
Costs (€)	19,636	19,373	19,059	19,034	18,934
QALYs	3.875	3.815	3.722	3.780	3.867
PRA-Driven Prasugrel					
Costs (€)	19,205	18,984	18,867	18,715	18,581
QALYs	3.891	3.831	3.738	3.796	3.883
ICER vs. PRA-Driven Prasugrel	Dominated	Dominated	Dominated	Dominated	Dominated

ICER=incremental cost-effectiveness ratio; QALY=quality-adjusted life-year; PRA=platelet reactivity assay; €=Euros

TCT-162

Universal Versus Platelet Reactivity Assay-Driven Use of P2Y12 Inhibitors in Acute Coronary Syndrome Patients: Cost-Effectiveness Analyses from Five European Perspectives

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Background: Platelet reactivity assays (PRAs) can predict patients' likely response to clopidogrel. We assessed the cost-effectiveness of universal compared to PRA-driven selection of ticagrelor or prasugrel for acute coronary syndrome (ACS) patients living in multiple European countries.
Methods: An Markov model was used to calculate 5-year costs (2013€), quality-adjusted life-years and incremental cost-effectiveness ratios (ICERs) for 1-year of universal ticagrelor or prasugrel (given to all) compared to each agents' corresponding PRA-driven strategy (ticagrelor/prasugrel in those with high platelet reactivity [HPR, >208 on the VerifyNow P2Y12 assay, Accumetrics, San Diego, CA], others given generic clopidogrel]. We assumed patients had their index ACS event at 65-70 years of age and had a 42.7% incidence of HPR post-revascularization. The analysis was conducted from the perspective of 5 different European countries (Germany, Italy, France, Spain and The Netherlands) and used a 1-year cycle length. Efficacy and safety data for P2Y12 Inhibitors were taken from multinational randomized trials and adjusted using country-specific epidemiologic data.
Results: Neither universal ticagrelor nor prasugrel were found to be cost-effective (all ICERs >40,250€/QALY) compared to their corresponding PRA-driven strategies in any of the countries evaluated (Table). Results were sensitive to differences in P2Y12 Inhibitors costs and drug-specific relative risks of major adverse cardiac events. Monte Carlo simulation suggested universal ticagrelor or prasugrel were cost-effective in only 29-44% and 11-17% of 10,000 iterations compared to their respective PRA-driven strategies, when applying a willingness-to-pay threshold=€30,000/QALY.
Conclusions: The universal use of newer P2Y12 inhibitors is not likely cost-effective compared to PRA-driven strategies.

TCT-163

Do Patients with Paroxysmal Atrial Fibrillation in Sinus Rhythm during PCI Require Triple Therapy? Results from a Multicenter Center Study

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Background: Paroxysmal atrial fibrillation (AF) is frequent in patients undergoing percutaneous coronary intervention (PCI), but optimum antithrombotic therapy has not been defined, and whether patients with paroxysmal AF in sinus rhythm (SR) at the time of PCI require anticoagulation concurrent with DAPT is unknown.
Methods: We evaluated 291 consecutive patients from 2 university Hospitals (US and Europe), with paroxysmal non-valvular AF who were in SR at the time of PCI between 2009 and 2011 prescribed triple (TT, n=98; 34%) or dual antithrombotic therapy (DAPT, n=193; 66%) post PCI and compared rates of major adverse cardiovascular events (MACCE = death, myocardial infarction [MI], revascularization, stroke, peripheral embolism or stent thrombosis) in patients on DAPT (aspirin + clopidogrel), vs. TT (DAPT + oral anticoagulant).
Results: Baseline characteristics in the TT and DAPT groups were similar for age (72 ± 9 vs. 70 ± 10 years; P=0.25), gender (29 vs. 27% females, P=0.73), CHA2DS2VASc score >1 (91 vs. 86%, P=0.25), and ejection fraction <30% (12 vs. 9%, P=0.34). The TT group had shorter lesions and stents compared to those on DAPT (25 ± 19 vs. 30 ± 19 mm, P=0.02). Mean duration of clopidogrel therapy was similar, as was the use of bare-metal stents. At 1-year, rates of MACCE (22 vs. 20%; P=0.71, Figure 1.), stroke (1.2 vs. 0.6%, P=0.13); major bleeding (3 vs. 1%, P=0.37)

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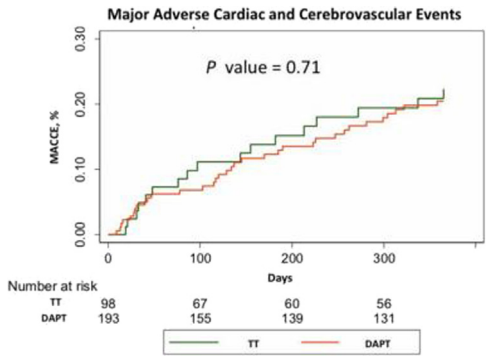
and net adverse cardiac events (25 vs. 21%, P=0.56) were similar in the TT and DAPT groups, respectively.
Conclusions: There does not seem to be a significant benefit of TT over DAPT in patients with paroxysmal AF in SR undergoing PCI.



TCT-164

Assessment of the efficacy of ex vivo platelet transfusion in the restoration of platelet function in acute coronary syndrome and PCI presenters treated with clopidogrel, prasugrel or ticagrelor – The APTITUDE study

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Background: The Antagonize P2Y12 Treatment Inhibitors by Transfusion of platelets in an Urgent or DElayed Timing after ACS or PCI presentation (The APTITUDE study) was designed to demonstrate the effect of ex vivo platelet transfusion (PT) in a coronary population receiving loading doses of P2Y12 receptor antagonists.
Methods: Patients presenting with acute coronary syndrome or for elective PCI and receiving a loading dose of either clopidogrel 600/900mg, prasugrel 60mg or ticagrelor 180mg were included. Blood was drawn from participants at two different time points; just before administration of the P2Y12 inhibitor loading dose (LD) (H0) and 4-6 hours after (H4). Transfusion was performed ex vivo by mixing naïve platelets in the form of platelet rich plasma (PRP-H0) with PRP at H4 (PRP-H4) in increasing proportions. The primary study endpoint was the percentage restoration of platelet function with addition of 80% proportion of PRP H0 measured by the residual platelet aggregation (RPA) in response to 20 µM ADP {RPA (80%/20% H0/H4 mix)/RPA baseline x 100} using light transmission aggregometry.
Results: A total of 56 patients (76% male) half (n=28) presenting with ACS and half presenting for elective PCI were included. Baseline RPA did not differ significantly between groups (p=0.65). Patients with poor pharmacodynamic response to the LD administered (RPA H4>46.6%) were excluded from the final analysis leaving 45 patients: Groups 1. clopidogrel 600mg (n =13) 2. clopidogrel 900mg (n=12) 3. prasugrel 60mg (n=10) 4. ticagrelor 180mg (n=10). Increasing proportions (30%, 50%, 80%) of platelet transfusion led to a stepwise increase in restoration of platelet reactivity in all groups 1-4 (p for trend < 0.0001, 0.01, <0.0001 and 0.0052 respectively). The primary endpoint of % restoration of platelet function with 80% proportion PT showed a stepwise decrease from groups 1 to 4 (83.9±11%, 73±14%, 66.3±15%, 40.9±19% respectively; p for trend < 0.0001).
Conclusions: The efficacy of ex vivo platelet transfusion in normalization of platelet function appears to decrease with more potent P2Y12 receptor antagonism and to be the least with direct P2Y12 inhibitors.

TCT-165

Ticagrelor vs Prasugrel maintenance dose in patients with acute coronary syndrome: a pharmacodynamic comparison

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Background: Data on direct pharmacodynamic comparison between ticagrelor and prasugrel are limited, mainly involving specific subgroups (e.g. patients with ST elevation myocardial infarction-STEMI, diabetes mellitus or high platelet reactivity under clopidogrel).
Methods: This was a prospective, single-center study, in consecutive patients with acute coronary syndrome (ACS), who underwent percutaneous coronary intervention (PCI). Platelet reactivity (PR) measurement was performed 30 days after constant treatment with ticagrelor 90mg bid or prasugrel 10mg od maintenance dose. Treatment choice was at physicians' discretion. Bleeding events (Bleeding Academic Research Consortium –BARC classification) were also monitored.
Results: We recruited 384 patients (with a mean age of 59.3±11.1 years, 83.6% men, 24.5% diabetics and 55.7% admitted with STEMI), out of them 211 and 173 received ticagrelor and prasugrel respectively. Demographic and angiographic characteristics of patients were well balanced between groups. After propensity score adjustment for gender, diabetes mellitus, smoking, creatinine clearance<60ml/min, age, hematocrit, platelet count and body mass index, PR at 30 days was significantly lower with ticagrelor compared with prasugrel (34.4, 95%CIs 28.2-40.7 versus 81.9, 95%CIs 74.9-88.8, p<0.001). There was a trend towards more BARC type 1 events with ticagrelor compared to prasugrel at 30 days (38.9% vs 29.5%, p=0.07). However, BARC type ≥2 events did not differ between ticagrelor and prasugrel (1.4% vs 2.9%, p=0.5).
Conclusions: In patients with ACS undergoing PCI, ticagrelor MD produces a significantly higher platelet inhibition compared to prasugrel MD. This observed pharmacodynamic difference might be associated with more nuisance bleeding events with ticagrelor use.

TCT-166

Correlates of High Platelet Reactivity on Clopidogrel in 8,533 Patients: An ADAPT-DES Substudy

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Background: Several studies have demonstrated an association between high platelet reactivity (HPR) on clopidogrel and the risk of stent thrombosis and adverse ischemic outcomes. We sought to determine the correlates of HPR from a large observational study of patients undergoing routine platelet reactivity testing.
Methods: ADAPT-DES was a prospective multicenter study of pts treated with coronary DES designed to determine the predictors of stent thrombosis. VerifyNow P2Y12 testing was performed after clopidogrel loading in 8,583 "all-comer" pts enrolled at 11 international sites. Linear regression of platelet reactivity units (PRU) on baseline and procedural covariates was used to determine independent correlates of PRU.
Results: The mean age was 63.6 years, an acute coronary syndrome was present in 51.7% of pts, and the mean PRU was 188 ± 97. Baseline demographic characteristics independently associated with higher PRU included: age, body mass index, female sex, non-Caucasian ethnicity, diabetes, non-smoking status, prior myocardial infarction, and anemia. Pre-hospital use of a thienopyridine or statin was independently associated with higher PRU. When procedural characteristics were examined in addition to baseline covariates, use of femoral vascular access, intra-aortic balloon pump, and bivalirudin for anticoagulation were all independently associated with higher PRU, as were baseline TIMI 0/1 flow, total stent length, and treatment of calcific lesions. Further modeling to identify the percent contribution of each of these covariates to the overall variance of PRU will be performed/presented.
Conclusions: In a large unselected cohort of patients undergoing PCI with DES, numerous independent correlates of HPR were identified, including demographic characteristics, comorbid conditions, antecedent medications, and procedural variables. These findings illustrate the multifactorial nature of clopidogrel responsiveness among patients undergoing PCI.

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